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CASE REPORT

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Pulmonal Bacillus Calmette-Guerin Infection 24 Months after Intravesical BCG Installation

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ABSTRACT

BCG (Bacillus Calmette-Guérin) immunotherapy is a method which is an emerging form of cancer treatment. BCG attaches to the bladder wall and stimulates an immune response to destroy the cancer cells. Complications of BCG therapy are due to reactivated infection or a hypersensitivity reaction and thus may be treated with antimycobacterial agents, corticosteroids, or both. BCG therapy instillations should also be stopped if complications occur during the treatment period. We present a case wherein a subject sufferef from a disseminated BCG infection 2 years after BCG instillation.

KEYWORDS: Bacillus Calmette-Guerin, BCG, Instillation, Mycobacterium

INTRODUCTION

Attenuated bacillus Calmette-Guerin (BCG), a live attenuated strain of Mycobacterium bovis, is used primarily for vaccination against tuberculosis (TB), but in some parts of the world BCG is also used for immunotherapy. BCG is used for treatment of low-grade urothelial tumors, in which case BCG is administered by intravesical instillation.[1] More than 95% of all patients tolerate this treatment well and experience no complications. The most common adverse events are local, mild, and self-limiting; serious events include systemic effects but they are very rare. Internationally, sepsis has been reported in approximately 0.4% and pneumonitis/hepatitis in approximately 0.7% of treated patients [1]. Risk factors for complications after BCG instillation include traumatic catheterization, cystitis, and poor immunological status.[1,2] Whether systemic disease after BCG flush is due to bacterial dissemination and/or hypersensitivity reaction is subject to ongoing debate.[2] The hypersensitivity theory is supported by the fact that patients respond well to glucocorticoids added to the anti-tuberculosis regimen, and that demonstration of bacteria is extremely uncommon.[1] However, the rare findings of BCG in tissue outside the bladder unarguably support the dissemination theory[2] and there is growing consensus that both mechanisms are valid.[2] This case report is about one of the few cases in which the diagnosis of disseminated BCG infection was verified through polymerase chain reaction (PCR) and culturing of BCG. Through genotyping it was possible to conclude that the patient's clinical disease was more than likely due to bacterial dissemination from the bladder.

CASE STUDY

A 64-year-old male was admitted to the hospital with pneumonia and signs of sepsis. He had severe COPD and papilloma of the bladder and was being monitored in a follow-up period after BCG instillations for these conditions. The patient was in poor general condition and had experienced unintended weight loss of 12-14 kg over 2-3 months prior to admission. He also had a personal history of over-consumption of alcohol. As the pneumonia was resistant to treatment, suspicion of TB was raised. The patient had been treated for pulmonary TB ten years earlier. Because of suspected recurrence of TB, two expectorate samples were sent to be tested for mycobacteria. On laboratory examination, acid-alcohol-fast bacilli were identified through auramine-rhodamine staining and PCR was positive for the M. tuberculosis complex, for which reason treatment was changed to four-drug standard tuberculosis therapy (isoniazid, rifampicin, ethambutol, and pyrazinamide). Surprisingly, culture and type determination subsequently found that this was Mycobacterium bovis BCG, and the patient was diagnosed with BCGitis. Through genotyping using the latest gold standard method mycobacterial interspersed repetitive unit variable number of tandem repeats[3], a known vaccine strain was identified which, in terms of genotype, was the strain used for BCG instillation two years earlier.

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DISCUSSION

There is only anecdotal reporting of culture-verified BCGitis[2], making this case study a challenge in terms of differential diagnosis, especially in the light of the patient's previous history of TB. But it is precisely through the patient's history that the suspicion of "BCGitis" was brought up, as it is known, that systemic disease can, albeit rarely, occur several years after a BCG instillation.[2] In all patients previously treated with BCG flushes, one must be aware of a possible connection with the patient's current condition, even if it has been many years since the patient was exposed to BCG. The patient in the case study was offered referral for immunological investigation but declined. In the light of his over-consumption of alcohol and poor general condition, it is not difficult to imagine that he had some level of compromised immune defense, which may have played a role in the activation of BCG, but this remains unknown.

The clinical consequence lies in the fact that BCG strains are naturally resistant to pyrazinamide and in some cases also to isoniazid. The strain in the case study was a BCG-medac, which is a RIVM derived strain 1173-P2. This strain is also pyrazinamide-resistant, but is fully sensitive to isoniazid, rifampin, rifabutin, ethambutol, and second-line anti-tuberculosis drugs.4 A rational therapeutic choice therefore demands that the correct diagnosis is obtained by sending appropriate samples to be tested for mycobacteria, even when there is confidence in the diagnosis on the basis of clinical assessments and medical history.

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